REMARKS/ARGUMENTS

Claims 1-35 are currently pending in the above-identified application. Claims 1-9, and 22-35 have been canceled from consideration as being directed to non-elected subject matter without prejudice to Applicants' right to prosecute the subject matter encompassed by the claims in a related, co-pending application. Claim 15 has been withdrawn from consideration in light of the request by the Examiner for a species election. Applicants request consideration of additional species once either the elected species or a generic claim has been found allowable. Claims 10 - 14, and 16- 21 remain pending. Claim 10 has been amended to set forth the present invention with greater particularity as set forth in detail below. Further, claims 16-18 and 20 have been amended to place the claims in present tense as requested by the Examiner. Claim 11 has been canceled as the subject matter of the claim has been included in the amendment to claim 10. Support for these amendments is identified above or in the following remarks. Applicants expressly reserve the right to prosecute any subject matter cancelled by the present amendments set forth herein in a related, co-pending application. The specification has been amended at page 1, line 21 to delete an extra comma. No new matter is added by any of the above amendments.

Rejections under 35 U.S.C. § 112

Claims 10, 12-14, and 16-21 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. In particular, the Examiner does not believe there is sufficient written description to show that Applicant was in possession of "a factor or agent that promotes Major Histocompatibility Complex- (MHC-) class I processing of the antigen other than BCG.

Although Applicants disagree that only BCG has been disclosed as an agent or factor that promotes MHC-class I processing of an antigen, claim 10 has been amended to recite "administering, to a patient in need thereof, an effective amount of human dendritic cells, exposed *in vitro* to an antigen and bacillus Calmette Guerin (BCG) or BCG with lipopolysaccharide (LPS) to promote Major Histocompatibility Complex- (MHC-) class I processing of the antigen" in order to further expedite prosecution of certain subject matter encompassed by the claims as originally filed. Claim 11 has been cancelled as the limitations of the claim have been incorporated into claim 10. The amendment of claim 10 is believed to obviate the rejection of claims 10, 12-14 and 16-21 under 35 U.S.C. § 112, first paragraph, and therefore, the Examiner is respectfully requested to withdraw the rejection of the claims on this basis.

Rejections under 35 U.S.C. §103

Claims 10-14 and 16-21 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,788,963 (the '963 patent) in view of Ramoner *et al.* (*J. Urol.* 159:1488-1492, 1998). The Examiner believes the '963 patent teaches a method for producing a tumor cell proliferation inhibiting response comprising administering to a patient an effective amount of human DCs, said DCs having been exposed *in vitro* to the prostate tumor associated antigenic fragment PSM-P1 (SEQ ID NO:1). The reference further teaches that the DCs are obtained from peripheral blood, have been cryopreserved, have been obtained from a healthy HLA matched donor, are extended life span, and can be administered to a metastatic prostate cancer patient. The difference between the reference and the claimed invention is believed by the Examiner to be that it does not teach the use of BCG in the *in vitro* exposure of the DCs to antigen. Further, the Examiner summarizes Ramoner *et al.* as teaching that BCG "is a potent activator of human DCs and that the reference further teaches that BCG stimulates the ability of DCs to activate T cells. In addition the Examiner alleges that Ramoner *et al.* teach that BCG could be used in DC based tumor immunotherapy.

On these basis the Examiner has concluded that "it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to perform a method for producing a tumor cell proliferation inhibiting response comprising administering to a patient an effective amount of human DCs, said DCs having been exposed *in vitro* to the prostate tumor associated antigenic fragment PSM-P1 (SEQ ID NO:1), said DCs having been obtained from peripheral blood, having been cryopreserved, having been obtained from a healthy HLA matched donor, having been extended life span, and having been administered to a metastatic prostate cancer patient, as taught by the '963 patent." The Examiner further states that "one of ordinary skill in the art would have been motivated to add BCG to the *in vitro* exposure of said DCs because BCG 'is a potent activator or human DCs', BCG stimulates the ability of DCs to activate T cells, and BCG could be used in DC based tumor immunotherapy, as taught by Ramoner *et al.*"

Applicants respectfully must disagree with the Examiner's conclusions relating to the cited Ramoner *et al.* reference and with its combination with the '963 patent. Applicants believe that the Examiner has failed to establish a *prima facie* basis for an obviousness rejection. To establish a *prima facie* case of obviousness, three basic criteria must be met by the Examiner. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine the teachings of the cited references. Second, there must be a reasonable expectation of success. Finally, the prior art references when combined must teach or suggest all of the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on the applicant's disclosure. *In re* Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

In this instance the Examiner has not taken into consideration all of the elements of the claims nor has any reasons for suggesting a reasonable basis for an expectation of success been provided. Claim 10 recites " exposed *in vitro* to an antigen and bacillus Calmette Guerin (BCG) or BCG with lipopolysaccharide (LPS) to promote Major Histocompatibility Complex-(MHC-) class I processing of the antigen." In the remarks of the Examiner stating the basis for

this rejection there is no discussion of the limitation that the exposure of the DCs to the antigen and BCG or BCG and LPS result in a MHC-class I response. In fact, Ramoner *et al.* do not disclose or suggest the use of BCG, or BCG with LPS, combined with an antigen can promote an MHC-class I response. Instead, Ramoner *et al.* teach that BCG induces a MHC-class II response in dendritic cells as measured by the proliferation of allogenic T cells. (See page 1491, right column, lines 11-13). It is well known in the art that a mixed lymphocyte response measures the proliferation of T cells after allogeneic stimulation is a marker for helper function (a class II response) in T cell immunity. See for example; page 1109, right column, first sentence in the section entitled "Alloreactive Helper Activation Measured In Vitro," *in* Fundamental Immunology, Third Edition, Paul, W.E. editor, Raven Press, New York, 1993, a copy of which is attached. Further, Ramoner *et al.* disclose that the "contact of dendritic cells with BCG strongly stimulates the pro-inflammatory cytokine tumor necrosis factor-α" which is known to be "an important maturation factor of human dendritic cells that has been shown to down regulate the endocytic mechanism serving antigen uptake and up regulate the T cell co-stimulatory activity of dendritic cells during their maturation." See Ramoner *et al.* page 1491, right column, lines 2-6. Still further, Ramoner *et al.* in summarizing their results state "BCG is a potent activator of human dendritic cells. It stimulates IL-8 production as well as the ability of dendritic cells to activate T cells. Such effects of BCG on the most potent antigen presenting cells in vivo would contribute to the observed antitumor effects of BCG in superficial bladder carcinoma." (See page 1491, right column, beginning the section entitled Conclusions). These teachings immediately precede the statement cited by the Examiner as the motivation for combining Ramoner *et al.* and the '963 patent in the present rejection. Applicants fail to see any reasons presented by the Examiner from within the references for their combination as the basis for the instant rejection.

For these reasons, Applicants believe that the Examiner has failed to make a *prima facie* case for obviousness by 1) not taking into consideration all of the elements of the claims and 2) not providing any reasonable expectation for success or a suggestion or motivation for concluding that the exposure *in vitro* of human DCs with an antigen and BCG or BCG and

LPS to promote MHC-class I processing of the antigen based on the teachings of Ramoner *et al.* either alone or in combination with the '963 patent. Even if the Examiner were considered to have met the burden of stating a proper *prima facie* case for obviousness, Applicants believe that the teaching of Ramoner *et al.* would at most suggest to the skilled artisan that BCG could be added as an *in vivo* adjuvant with the activated DCs taught by the '963 patent. This is not the claimed invention. Further, the teachings of Ramoner *et al.* only establish that BCG activates a MHC-class II response in DCs and provides no disclosure or suggestion relating to the induction of a MHC-class I response. Applicants therefore respectfully request the Examiner withdraw the present rejection of claims 10-14 and 16-21 under 35 U.S.C. § 103(a) as being unpatentable over US Patent 5,788,963 in view of Ramoner *et al.*

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 206-467-9600.

Respectfully submitted,

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